

## HV interval in calcific aortic stenosis

### *Relation to left ventricular function and effect of valve replacement*

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**SUMMARY** Intracardiac electrography and 24 hour ambulatory electrocardiographic monitoring were carried out in 20 patients with calcific aortic stenosis (mean pressure gradient 86 mm Hg) to investigate (a) the role of bradycardia and tachycardia in the pathogenesis of syncope in aortic stenosis, (b) the relation between haemodynamic data and electrophysiological abnormalities, and (c) whether valve replacement corrects electrophysiological abnormalities. Intracardiac electrograms showed impaired sinus node function in five patients and a prolonged HV interval ( $\geq 50$  ms) in 11 but there was no difference in the findings of 13 patients with syncope and seven without. Ambulatory monitoring showed short pauses in three patients and brief episodes of tachycardia in four, but there was no difference in the findings of patients with and without syncope. The HV interval correlated inversely with the left ventricular ejection fraction, whereas no correlation was found between the HV interval and the pressure gradient. Nine patients were re-evaluated 15 months after aortic valve replacement. No change was found in sinus node function, but the HV interval had increased by 7.8 ms.

It is concluded that in calcific aortic stenosis neither bradycardia nor tachycardia is shown to be a frequent cause of syncope, a prolonged HV interval is a frequent finding and further prolongation occurs after valve replacement, and contractility and conductivity appear to deteriorate in parallel.

In 1935 Boas reported complete heart block in two patients with aortic stenosis,<sup>1</sup> and in the same year Yater and Cornell demonstrated histopathologically the invasion and destruction of the bundle of His by calcium deposits extending from the adjacent calcified aortic valve.<sup>2</sup> In 1954 Mitchell *et al* reported atrio-ventricular block or bundle branch block in 26% of 455 patients with aortic stenosis.<sup>3</sup> Thus the relation between aortic stenosis and conduction disturbances is well established.

Recent intracardiac electrophysiological studies in aortic stenosis have shown increased HV intervals in 27-75% of patients,<sup>4,5</sup> indicating latent disease of the His-Purkinje system. Conflicting opinions, however,

exist on the clinical relevance of this finding. Dhingra *et al* suggested that, owing to intermittent atrioventricular block, a prolonged HV interval might be associated with syncope in aortic stenosis,<sup>4</sup> whereas Gann *et al* concluded that conduction disorders are rarely responsible for syncope in aortic stenosis.<sup>5</sup>

Electrocardiographic evidence of atrioventricular block with bradycardia during syncope in aortic stenosis has been provided by Schwartz *et al*, who have also reported syncopal attacks associated with ventricular tachycardia in such patients.<sup>6</sup>

The aim of the present study using intracardiac electrography and ambulatory monitoring was to determine whether paroxysmal bradycardia or tachycardia or both is likely to be a frequent cause of syncope in aortic stenosis and whether electrophysiological abnormalities are related to haemodynamic findings. Furthermore, we aimed to determine whether valve replacement corrected electrophysiological abnormalities, which to our knowledge has not been studied previously.

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Table 1 Clinical and haemodynamic data and preoperative electrophysiological data in 20 patients with calcific aortic stenosis. Figures in parentheses are postoperative data

Case no.	Age (yr) and sex	Syncope	ECG findings (post-operative)	Pressure gradient (mm Hg)	EF (%)	LVEDP (mm Hg)	Stenosed vessel	Conduction intervals				SRT:SCL ratio	SACT (ms)	Ambulatory monitoring	Surgical follow up (months)
								AHRA-AHBE (ms)	AH (ms)	HV (ms)					
* 68 M		Yes	RBBB	37	—	16	—	20	100	70	1-23	115	Normal		
* 66 M		Yes	LVH	98	75	25	—	35	130	50	1-18	163	VT, SVT		14
										(45)	(1-55)				
* 40 M		No	LVH	116	62	34	—	20	90	60	1-31	97	Normal		18
			(LBBB)							(75)	(1-28)				
* 69 M		Yes	LVH	100	62	17	—	40	90	45	1-09	—	Normal		18
										(50)	(1-29)				
* 69 F		Yes	LVH	111	74	14	—	40	60	50	1-03	74	Normal		
* 56 F		No	LVH	96	85	11	None	30	95	45	1-31	—	Normal		18
										(60)	(1-07)				
* 64 M		No	LAFB	96	49	29	—	40	120	60	1-33	61	Normal		18
			(RBBB)							(60)	(1-34)				
53 M		Yes	LVH	45	75	10	—	40	60	40	1-53	—	Pause (1-6s)		
62 F		No	Normal	50	70	20	None	—	95	45	1-18	58	Normal		
* 57 M		Yes	LVH	70	65	8	LAD, RCA, LCX	20	70	45	1-27	83	Normal		16
			(LAFB+RBBB)							(55)					
59 M		Yes	CHB	120	51	20	—	25	110	†	—	—	CHB		
62 M		No	LVH	76	55	16	LAD, RCA	30	90	60	1-41	—	SVT		
* 66 M		Yes	LVH	70	85	26	—	25	130	45	1-64	230	Pause (1-8s)		
			(LAFB)							(45)	(1-37)				
* 69 M		Yes	LAFB+RBBB	90	—	25	LAD, RCA	40	85	65	1-22	148	Normal		14
			(LAFB)							(70)	(1-37)				
64 F		No	LVH	128	61	45	None	30	140	45	1-35	263	Pause (2-8s)		
* 39 M		Yes	LVH	97	—	9	—	40	115	40	1-21	—	Normal		9
			(LBBB)							(65)	(1-06)				
47 M		No	LVH	83	42	32	None	25	115	70	1-12	49	Normal		
68 M		Yes	LVH	64	77	14	LAD, RCA, LCX	18	110	35	1-32	85	Normal		
65 M		Yes	LBBB	100	43	24	None	30	130	65	1-17	85	AF		
68 M		Yes	LAFB+RBBB	64	43	48	LAD	20	95	60	1-25	43	VT, SVT		
mean 60-6				85-6	63-2	22-2		30-0	105-5	52-4	1-27	111-0			15-4
										(58-3)	(1-29)				
SD 9-3				25-4	14-3	11-2		8-2	27-9	10-8	0-15	67-3			3-0
										(10-6)	(0-16)				

\*Underwent re-evaluation. EF, ejection fraction; LVEDP, left ventricular end diastolic pressure; LVH, left ventricular hypertrophy; CHB, complete heart block; LAFB, left anterior fascicular block; RBBB, right bundle branch block; LBBB, left bundle branch block; LAD, left anterior descending coronary artery; RCA, right coronary artery; LCX, left circumflex coronary artery; VT, ventricular tachycardia; SVT, supraventricular tachycardia; AF, atrial fibrillation.

†Had complete infra-His block.

## Patients and methods

We studied 20 consecutive symptomatic patients with calcific aortic stenosis without signs of aortic regurgitation and without involvement of other valves. Thirteen patients had syncopal episodes and seven had no history of syncope but had either chest pain or cardiac decompensation. Nineteen patients were in sinus rhythm, and one patient had complete heart block. The Table shows the clinical data.

### PRESSURE GRADIENT AND EJECTION FRACTION

Left heart catheterisation was performed in all the patients using either the retrograde or transseptal technique. From the pressure recordings the peak to peak gradient across the aortic valve was determined.

Left ventricular function was assessed by M mode echocardiography. In 16 patients a satisfactory recording was obtained, and the left ventricular ejection

fraction (EF) was calculated according to the following formula:

$EF (\%) = 100 \times (LVIDD^3 - LVIDS^3) / LVIDD^3$ , where LVIDD is the left ventricular internal diameter in diastole and LVIDS the left ventricular internal diameter in systole, as previously described by Pombo *et al.*<sup>7</sup> In four patients no satisfactory echocardiogram was obtained, and in one of these the ejection fraction was calculated from a biplane left ventriculogram (30° right anterior oblique and 60° left anterior oblique projections) from which two short and one long ventricular diameters were measured in diastole and systole and volumes calculated using the formula for an ellipsoid. In three patients no ejection fraction could be determined.

### CORONARY ANGIOGRAPHY

Coronary angiography was performed in all 10 patients with chest pain, and in five significant

stenosis (>50% diameter reduction in at least one vessel) was found. The haemodynamic and angiographic data are shown in the Table.

#### INTRACARDIAC ELECTROGRAPHY

A few days after the haemodynamic evaluation intracardiac electrography was performed, as previously described.<sup>8</sup> Briefly, intracardiac electrograms were recorded using two hexapolar pacing wires introduced via a femoral vein under local anaesthesia. One pacing wire was placed in the high right atrium and the other across the tricuspid valve in a position that gave a well defined H potential. During spontaneous sinus rhythm the following conduction intervals were measured with a paper speed of 100 mm/s: (a) the intra-atrial conduction time ( $A_{HRA} - A_{HBE}$ , where  $A_{HRA}$  is the A potential in the HRA electrogram and  $A_{HBE}$  the A potential in the His bundle electrogram), (b) the atrioventricular nodal conduction time (AH), and (c) the infra-nodal conduction time (HV). All conduction intervals were expressed in milliseconds (ms) and were measured to the nearest 5 ms. Atrial pacing was performed for one minute at rates of 90, 110, and 130 beats/minute, and sinus node function was expressed as the ratio of sinus recovery time (SRT) to sinus cycle length (SCL). Sinoatrial conduction time (SACT) was determined as described by Strauss *et al.*<sup>9</sup> We use the following reference values in this laboratory:  $A_{HRA} - A_{HBE} < 55$  ms, AH < 140 ms, HV < 50 ms, SRT:SCL ratio < 1.48, and SACT < 130 ms.<sup>8</sup>

#### AMBULATORY MONITORING

Twenty-four hour Holter ambulatory monitoring was performed in all patients with a two channel Oxford Medilog tape recorder, and the tapes were analysed with a semiautomatic arrhythmia analyser (Reynolds Pathfinder). We noted the occurrence of the following arrhythmias: ventricular tachycardia (episodes of at least three consecutive ventricular extrasystoles), supraventricular tachycardia (episodes of at least three consecutive supraventricular extrasystoles), atrial fibrillation, and pauses with RR intervals > 1.5 s (excluding compensatory pauses after premature QRS complexes).

#### VALVE REPLACEMENT

Valve replacement was performed during extracorporeal circulation and Brettschneider cardioplegia. During the study period Starr-Edwards and St Jude mechanical prosthetic valves were implanted. Post-operative electrograms were recorded in patients after they had given written informed consent with the identical technique to that used preoperatively. Left heart catheterisation, echocardiography, and ambulatory monitoring were not performed post-

operatively.

#### STATISTICAL ANALYSIS

Statistical analysis was performed with the *t* test for paired or unpaired data, whichever was appropriate, and linear regression analysis with the least squares method. A *p* value of < 0.05 was considered statistically significant.

#### Results

##### ELECTROPHYSIOLOGICAL FINDINGS

The preoperative electrophysiological findings are shown in the Table. The intra-atrial conduction time was normal in all and the AH interval normal in all except one patient (case 15), who had a slightly prolonged AH interval. Sinus node function was abnormal in five patients, two having an increased SRT:SCL ratio and four a prolonged SACT. The HV interval was prolonged in 11 (55%) patients, of whom one had a third degree infra-His block. No patients developed second or third degree intra-His or infra-His block during atrial pacing.

There was no significant difference in the SRT:SCL ratio between the 13 patients with a history of syncope (mean 1.29) and the seven without syncope (mean 1.29) or in the HV interval between patients with syncope (mean 51 ms) and those without (mean 55 ms).

The results of ambulatory monitoring are shown in the Table. Of the 13 patients with syncope, pauses or tachycardias were seen in five (38.5%) compared with two of the seven (28.6%) patients without syncope; this difference was not significant. The pauses were all due to sinoatrial block and were found in patients who had signs of sinus node dysfunction by intra-cardiac electrography. The episodes of ventricular and supraventricular tachycardia were of short duration (maximum eight consecutive extrasystoles) and were not associated with cerebral symptoms.

There was no significant correlation between the HV interval and the pressure gradient ( $r = 0.01$ ), and no significant correlation between the HV interval and the left ventricular end diastolic pressure ( $r = 0.41$ ,  $p = 0.07$ ) whereas the HV interval was significantly correlated to the ejection fraction ( $r = -0.82$ ,  $p < 0.001$ ,  $n = 16$ ; Fig. 1).

##### VALVE REPLACEMENT

Valve replacement was performed in 18 patients, of whom 10 received a Starr-Edwards prosthesis (size 10–13) and eight a St Jude prosthesis (size 21–31); two patients died in heart failure before operation. After operation the patient with third degree infra-His block preoperatively died suddenly despite permanent pacemaker treatment. (Necropsy did not identify

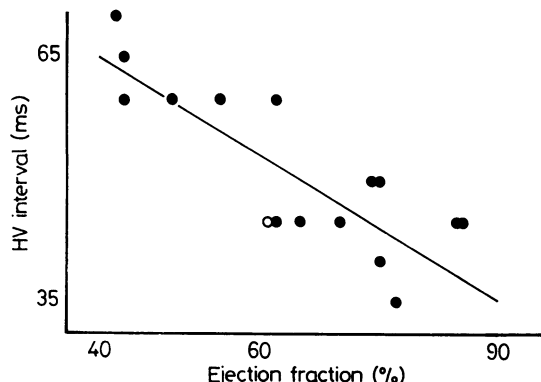


Fig. 1 HV interval (ms) and left ventricular ejection fraction determined by echocardiography (●) and by ventriculography (○) in 16 patients with calcific aortic stenosis ( $r = -0.81$ ,  $p < 0.001$ ).

the cause of death.)

Because of sinus arrest with a 4 s asystole a pacemaker was implanted in one patient (case 15) a month after operation. The remaining 16 patients were considered to be possible candidates for repeat electrophysiology, which was performed in 10 patients who gave signed informed consent but failed in one (case 1), who developed atrial fibrillation during insertion of the pacing wires. Thus complete re-evaluation

was achieved in only nine patients an average of 15 (range 9–18) months after operation.

The results of the postoperative electrograms are shown in the Table. (We did not determine the SACT postoperatively since these data were missing in the preoperative study in three of the nine patients, and we have not shown the  $A_{HRA} - A_{HBE}$  and the AH intervals since these findings were generally normal before and after operation.) The postoperative study showed no change in the SRT:SCL ratio (preoperative mean 1.29, SD 0.16, postoperative mean 1.29, SD 0.16), but a significant increase was found in the HV interval after operation (preoperative mean 50.5 ms, SD 8.8, postoperative mean 58.3 ms, SD 10.6,  $p < 0.05$ ) (Table, Fig. 2).

The HV interval increased in all six patients with surgical bundle branch block or fascicular block (Table). None of the 13 patients with syncope before operation had syncopal attacks after operation (mean follow up time 15 (range 3–20) months).

## Discussion

In this study we found a high incidence of electrophysiological abnormalities in 20 patients with aortic stenosis since 55% had a prolonged HV interval and 25% sinus node dysfunction. These abnormalities were not, however, more pronounced in patients with syncope than in those without. Consequently our results do not support the hypothesis of Dhingra *et al*<sup>4</sup> that latent disease of the His-Purkinje system is associated with syncope in aortic stenosis, and the fact that the syncopal attacks disappeared after operation in all patients despite persistent postoperative prolongation of the HV interval is a strong argument against such a hypothesis. Furthermore, the intracardiac electrogram did not suggest that dysfunction of the sinus node was a frequent cause of syncope in aortic stenosis, and this conclusion is supported by the result of the ambulatory monitoring, which showed short pauses without symptoms in only two of the 13 patients with syncope (Table).

A complete electrophysiological evaluation of the mechanism of syncope in aortic stenosis would have included programmed atrial and ventricular stimuli to provoke tachycardia in patients with spontaneous attacks. We did not include such procedures in this study since we did not consider it to be ethically justified to induce tachycardia in patients with severe aortic stenosis. The ambulatory recordings did not, however, suggest that spontaneous attacks of tachycardia are a frequent cause of syncope in aortic stenosis since only three of the 13 patients with syncope had episodes of tachycardia, which were short and without cerebral symptoms.

Our results suggest that neither bradycardia nor

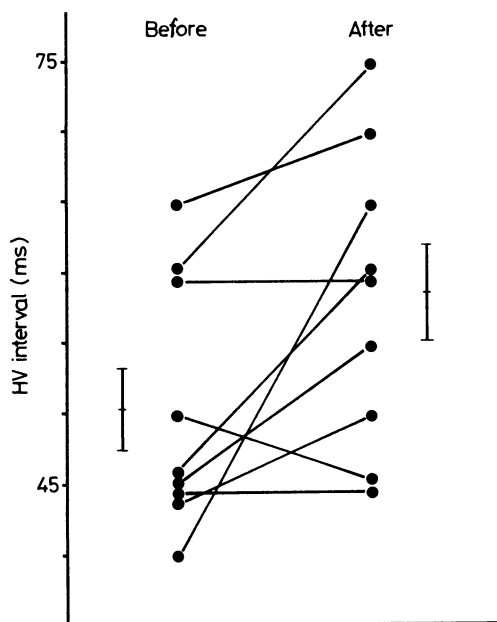


Fig. 2 HV intervals (ms) (mean (SEM)) in nine patients with calcific aortic stenosis before and after valve replacement. Mean postoperative increase was 7.8 ms ( $p < 0.05$ ).

tachycardia play a major role in the pathogenesis of syncope in aortic stenosis. Thus we consider that the initiating mechanism is more likely to be haemodynamic, sometimes with arrhythmias as a secondary phenomenon as described by Schwartz *et al.*<sup>6</sup>

Dhingra *et al.*<sup>4</sup> found significantly longer HV intervals in patients with a pressure gradient >40 mm Hg than in those with a gradient <40 mm Hg. In the present study in which only one patient had a gradient <40 mm Hg the HV interval was unrelated to the gradient, which agrees with the findings of Gann *et al.*<sup>5</sup>

The postoperative electrograms showed that valve replacement did not normalise the HV interval, which suggests that the disease of the His-Purkinje system is irreversible. The increase in the HV interval after operation in six patients was probably the result of surgical trauma to the conduction system as described by Follath and Ginks.<sup>10</sup> (For this reason we considered it inappropriate to relate the postoperative HV interval to the postoperative ejection fraction.)

It is generally known that the HV interval is often prolonged in calcific aortic stenosis,<sup>4,5</sup> but to our knowledge it is a new observation that the HV interval is inversely related to the ejection fraction. This relation may be difficult to understand if the HV interval prolongation is due only to a local (impairment) of the conduction system by the pathological process in the valve itself, as described by Boas.<sup>1</sup> We therefore think that an alternative explanation should be given for the relation between the HV interval and the ejection fraction. Levin *et al.* studied children with congenital aortic stenosis (presumably uncalcified) and found that the HV interval correlated positively with the systolic left ventricular pressure,<sup>11</sup> which suggests that the pressure load on the left ventricle may in itself cause a prolonged HV interval. This assumption is further substantiated by the report of Scheinman *et al.*, who found a high percentage of patients with arterial hypertension in a large series of patients with prolonged HV intervals.<sup>12</sup> If it is correct that a longstanding pressure load on the left ventricle can in itself damage the conduction system then it is not surprising that a parallel deterioration of conductivity and contractility may occur, since the longstanding pressure load is also responsible for the loss of contractility in aortic stenosis.

Several studies suggest that a relation between contractility and conductivity is not confined to aortic stenosis. Scheinman *et al.* reported a significantly higher percentage of patients with a prolonged HV interval in patients with heart failure than in those with a normal HV interval in a series of patients with bundle branch block mainly due to coronary and hypertensive heart disease.<sup>12</sup> Furthermore, Hamby *et al.* showed a relation between left ventricular function and disease of the conduction system in patients with coronary heart disease.<sup>13</sup>

In the present study all the three patients who died had a prolonged HV interval, but our data do not allow any conclusions to be drawn on the long term prognostic significance of a prolonged HV interval in aortic stenosis. Since there appears to be an association between a prolonged HV interval and impaired left ventricular function the former would seem to imply a poor prognosis. Whether or not a long HV interval is an independent risk factor in aortic stenosis has, however, never been specifically studied in a large population. In previous studies a prolonged HV interval seems to have implied a significantly increased mortality and an increased risk of progression to third degree atrioventricular block in patients with organic heart disease and bifascicular block or bundle branch block or both.<sup>12,14</sup> According to Scheinman *et al.*, however, only patients with an HV interval  $\geq 70$  ms had an increased risk, whereas the prognosis of patients with an HV interval between 55 and 70 ms did not differ from that of patients with a normal HV interval.<sup>12</sup> Since the HV interval is only moderately prolonged in aortic stenosis and after aortic valve replacement, it appears to be of only minor prognostic importance in these patients.

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